

## PATENT COOPERATION TREATY

2458-4042 PC

From the INTERNATIONAL BUREAU

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PCT

NOTIFICATION CONCERNING  
SUBMISSION OR TRANSMITTAL  
OF PRIORITY DOCUMENT

(PCT Administrative Instructions, Section 411)

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Date of mailing (day/month/year) 23 October 2000 (23.10.00)	
Applicant's or agent's file reference 2458-4042PC ✓	IMPORTANT NOTIFICATION
International application No. PCT/US00/17540 ✓	International filing date (day/month/year) 26 June 2000 (26.06.00) ✓
International publication date (day/month/year) Not yet published	Priority date (day/month/year) 25 June 1999 (25.06.99) ✓
Applicant GENAISSANCE PHARMACEUTICALS, INC. et al	

- The applicant is hereby notified of the date of receipt (except where the letters "NR" appear in the right-hand column) by the International Bureau of the priority document(s) relating to the earlier application(s) indicated below. Unless otherwise indicated by an asterisk appearing next to a date of receipt, or by the letters "NR", in the right-hand column, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).
- This updates and replaces any previously issued notification concerning submission or transmittal of priority documents.
- An asterisk(\*) appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b). In such a case, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.
- The letters "NR" appearing in the right-hand column denote a priority document which was not received by the International Bureau or which the applicant did not request the receiving Office to prepare and transmit to the International Bureau, as provided by Rule 17.1(a) or (b), respectively. In such a case, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

Priority date	Priority application No.	Country or regional Office or PCT receiving Office	Date of receipt of priority document
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The International Bureau of WIPO 34, chemin des Colombettes 1211 GENEVA 20, Switzerland	Authorized officer Magda BOUACHA
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17/00, G01N 33/48, 33/50, G06T 1/00

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(21) International Application Number: PCT/US00/17540

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HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
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— With international search report.

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*For two-letter codes and other abbreviations, refer to the "Guid-  
ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.*

(54) Title: METHODS FOR OBTAINING AND USING HAPLOTYPE DATA

(57) Abstract: Methods, computer program(s) and database(s) to analyze and make use of gene haplotype information. These in-  
clude methods, program, and database to find and measure the frequency of haplotypes in the general population; methods, program,  
and database to find correlation's between an individual's haplotypes or genotypes and a clinical outcome; methods, program, and  
database to predict an individual's haplotypes from the individual's genotype for a gene; and methods, program, and database to  
predict an individual's clinical response to a treatment based on the individual's genotype or haplotype.

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## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US00/17540

### B. FIELDS SEARCHED

Electronic data bases consulted (Name of data base and where practicable terms used):

DIALOG (files 5, 155) and EAST (files U.S. Patents, European abstracts, Japanese abstracts, and Derwent) search terms: pharmacogenomic, pharmacogenetic, haplotype, genotype, database, computer, clinical trial, population genetics, polymorphism, SNP, Hardy-Weinberg, Mendelian, linkage, phylogenetic, pedigree, locus, gene, phased, unphased

### BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING

This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

- Group I, claim(s) 1-8, 69-72, and 120-124, drawn to a method of generating a haplotype database, computer-usable medium, and computer programmed therefore.
- Group II, claim(s) 9-12 and 73, drawn to a method of predicting the presence of a haplotype and computer-usable medium therefore.
- Group III, claim(s) 13-21, 74-78, and 125-129, drawn to a method of identifying correlation between haplotype pair and clinical response, computer-usable medium, and computer programmed therefore.
- Group IV, claim(s) 22-29, 79-82, 130-133, drawn to a method for determining susceptibility to a condition/disease, computer-usable medium, and computer programmed therefore.
- Group V, claim(s) 30-33, 83-84, and 134-135, drawn to a method for predicting response to treatment, computer-usable medium, and computer programmed therefore.
- Group VI, claim(s) 34, 85, and 136, drawn to a method for generating a tree structure, computer-usable medium, and computer programmed therefore.
- Group VII, claim(s) 35, 86, and 137, drawn to a method for displaying haplotype pair frequency, computer-usable medium, and computer programmed therefore.
- Group VIII, claim(s) 36-37, 87-88, and 138-139, drawn to a method for displaying a linkage screen, computer-usable medium, and computer programmed therefore.
- Group IX, claim(s) 38-40, 89-91, and 140-142, drawn to a method for displaying a phylogenetic tree screen, computer-usable medium, and computer programmed therefore.
- Group X, claim(s) 41-42, 92-93, and 143-144, drawn to a method for displaying genotypic analysis, computer-usable medium, and computer programmed therefore.
- Group XI, claim(s) 43-51, 94-102, and 145-153, drawn to a method to displaying clinical response values, computer-usable medium, and computer programmed therefore.
- Group XII, claim(s) 52, 103, and 154, drawn to a method for carrying out a genetic algorithm, computer-usable medium, and computer programmed therefore.
- Group XIII, claim(s) 53, 104, and 155, drawn to a method for displaying correlations, computer-usable medium, and computer programmed therefore.
- Group XIV, claim(s) 54-55, 105-106, and 156-157, drawn to a method for conducting a clinical trial, computer-usable medium, and computer programmed therefore.
- Group XV, claim(s) 56-58, 107-109, and 158-160, drawn to a method for inferring genotype, computer-usable medium, and computer programmed therefore.
- Group XVI, claim(s) 59-63, 110-119, and 161-170, drawn to a method of determining polymorphic sites or subhaplotypes, computer-usable medium, and computer programmed therefore.
- Group XVII, claim(s) 171-175 and 183, drawn to a data structure.
- Group XVIII, claim(s) 176-182, drawn to a method for storing and organizing biological information.

The inventions listed as Groups I-XVIII do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The special technical feature of each method is the starting materials, method steps, and goal of each method. The corresponding computer-usable medium and computer programmed therefore form part of the inventive concept with each method. Note that PCT Rule 13 does not provide for multiple methods or products.

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US00/17540

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(8)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2. ☐ Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
  
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
  
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
  
3. ☒ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:  
1-21,30-33,35,43-51,53-58,69-78,83-84,86,94-102,104-109,120-129,134-135,137,145-153,155-160,171-183
  
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☒ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## INTERNATIONAL SEARCH REPORT

 International application No.  
PCT/US00/17540

## C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	CLARK et al. Haplotype Structure and Population Genetic Inferences from Nucleotide-Sequence Variation in Human Lipoprotein Lipase. American Journal of Human Genetics. 1998, Vol. 63, pages 595-912, see entire document.	1-21,30-33,35,43- 51,53-58,69-78,83- 84,86,94-102,104- 109,120-129,134- 135,137,145-15 3,155-160,171-183
Y	CASHMAN et al. The Irish cystic fibrosis database. Journal of Medical Genetics. 1995, Vol. 32, No. 12, pages 972-975, see entire document.	1-21,30-33,35,43- 51,53-58,69-78,83- 84,86,94-102,104- 109,120-129,134- 135,137,145- 153,155-160,171- 183
Y, P	TISHKOFF et al. The Accuracy of Statistical Methods for Estimation of Haplotype Frequencies: An Example from the CD4 Locus. American Journal of Human Genetics. August 2000, Vol. 67, No. 2, pages 518-522, see entire document.	1-21,30-33,35,43- 51,53-58,69-78, 83- 84,86,94-102,104- 109,120-129,134- 135,137,145- 153,155-160,171- 183
Y	PERLIN et al. Toward Fully Automated Genotyping: Allele Assignment, Pedigree Construction, Phase Determination, and Recombination Detection in Duchenne Muscular Dystrophy. American Journal of Human Genetics. 1994, Vol. 55, No.4, pages 777-787, see entire document.	1-21,30-33,35,43- 51,53-58,69-78,83- 84,86,94-102,104- 109,120-129,134- 135,137,145- 153,155-160,171- 183
Y	HOANG et al. PAH Mutation Analysis Consortium Database: A Database for Disease-producing and Other Allelic Variation at the Human PAH Locus. Nucleic Acids Research. 1996, Vol. 24, No. 1, pages 127-131, see entire document.	1-21,30-33,35,43- 51,53-58,69-78,83- 84,86,94-102,104- 109,120-129,134- 135,137,145- 153,155-160, 171- 183
Y, P	STEPHENS et al. Single-nucleotide Polymorphisms, Haplotypes, and Their Relevance to Pharmacogenetics. Molecular Diagnosis. December 1999, Vol. 4, No. 4, pages 309-317, see entire document.	1-21,30-33,35,43- 51,53-58,69-78,83- 84,86,94-102,104- 109,120-129,134- 135,137,145- 153,155-160, 171- 183

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US00/17540

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	KLEYN et al. Genetic Variation as a Guide to Drug Development. <i>Science</i> . 18 September 1998, Vol. 281, pages 1820-1821, see entire document.	1-21,30-33,35,43-51,53-58,69-78,83-84,86,94-102,104-109,120-129,134-135,137,145-153,155-160,171-183
Y	MORI et al. HLA Gene and Haplotype Frequencies in the North American Population. <i>Transplantation</i> . 15 October 1997, Vol. 64, No. 7, pages 1017-1027, see entire document.	1-21,30-33,35,43-51,53-58,69-78,83-84,86,94-102,104-109,120-129,134-135,137,145-153,155-160,171-183
Y	MORI et al. Computer program to predict likelihood of finding an HLA-matched donor. Methodology, validation, and application. <i>Biology of Blood and Marrow Transplantation</i> . October 1996, Vol. 2, pages 134-144, see entire document.	1-21,30-33,35,43-51,53-58,69-78,83-84,86,94-102,104-109,120-129,134-135,137,145-153,155-160,171-183
Y	MATISE, T. C. Genome Scanning for Complex Disease Genes Using the Transmission/Disequilibrium Test and Haplotype-based Haplotype Relative Risk. <i>Genetic Epidemiology</i> . 1995, Vol. 12, No. 6, pages 641-645, see entire document.	121,30-33,35,43-51,53-58,69-78,83-84,86,94-102,104-109,120-129,134-135,137,145-153,155-160,171-183
Y	COOPER et al. Network Analysis of Human Y Microsatellite Haplotypes. <i>Human Molecular Genetics</i> . 1996, Vol. 5, No. 11, pages 1759-1766, see entire document.	1-21,30-33,35,43-51,53-58,69-78,83-84,86,94-102,104-109,120-129,134-135,137,145-153,155-160,171-183
Y	GENE et al. Haplotype frequencies of eight Y-chromosome STR loci in Barcelona (North-East Spain). <i>International Journal of Legal Medicine</i> . 1999, Vol. 112, pages 403-405, see entire document.	1-21,30-33,35,43-51,53-58,69-78,83-84,86,94-102,104-109,120-129,134-135,137,145-153,155-160,171-183



## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US00/17540

## C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,773,220 A (DEKOSKY ET AL) 30 June 1998 (30-06-98), see in particular abstract and claims.	1-21,30-33,35,43-51,53-58,69-78,83-84,86,94-102,104-109,120-129,134-135,137,145-153,155-160,171-183
Y, P	US 5,972,614 A (RUANO ET AL) 26 October 1999 (26-10-99), see in particular abstract; claims; column 6, lines 33-55; column 12, lines 10-25.	1-21,30-33,35,43-51,53-58,69-78,83-84,86,94-102,104-109,120-129,134-135,137,145-153,155-160, 171-183
Y, P	US 6,022,683 A (POIRIER) 08 February 2000 (08-02-00), see in particular abstract and claims.	1-21,30-33,35,43-51,53-58,69-78,83-84,86,94-102,104-109,120-129,134-135,137,145-153,155-160, 171-183
Y, P	US 6,043,040 A (ACTON) 28 March 2000 (28-03-00), see in particular abstract, claims, and columns 49-59.	1-21,30-33,35,43-51,53-58,69-78,83-84,86,94-102,104-109,120-129,134-135, 137,145-153,155-160,171-183
Y	US 5,648,482 A (MEYER) 15 July 1997 (15-07-97), see in particular abstract, claims, and columns 23-26.	1-21,30-33,35,43-51,53-58,69-78,83,84,86,94-102,104-109,120-129,134-135,137,145-153,155-160,171-183
Y, P	US 6,030,778 A (ACTON ET AL) 29 February 2000 (29-02-00), see in particular abstract, claims, and columns 25-30.	1-21,30-33, 35,43-51,53-58,69-78,83-84,86,94-102,104-109,120-129,134-135,137,145-153,155-160,171-183

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US00/17540

## A. CLASSIFICATION F SUBJECT MATTER

IPC(7) : G06F 7/00, 17/00; G01N 33/48, 33/50; G06T 1/00

US CL : 345/418, 981; 702/19, 20; 707/100, 102, 104

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 345/418, 981; 702/19, 20; 707/100, 102, 104

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Please See Extra Sheet.

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,874,256 A (BERTINA ET AL) 23 February 1999 (23-02-99), see in particular abstract and claims.	1-21,30-33, 35,43-51, 53-58, 69-78,83-84,86,94-102,104-109,120-129, 134-135, 137,145-153,155-160,171-183

☒ Further documents are listed in the continuation of Box C.
 ☐ See patent family annex.

* Special categories of cited documents:	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E" earlier document published on or after the international filing date	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"I" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Z" document member of the same patent family
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Date of the actual completion of the international search

14 NOVEMBER 2000

Date of mailing of the international search report

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